



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,293	01/09/2001	Thomas E. Wagner	035879-0116	5976

7590 12/20/2002

FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W., Suite 500
P.O. Box 25696
Washington, DC 20007-8696

[REDACTED] EXAMINER

LI, QIAN J

ART UNIT	PAPER NUMBER
1632	18

DATE MAILED: 12/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/756,293	WAGNER ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 24 October 2002.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-15 and 17-31 is/are pending in the application.
- 4a) Of the above claim(s) 1-13 and 23-28 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 14,15,17-22 and 29-31 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 09 January 2001 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

The amendment and response filed 10/24/02 has been entered as paper #11.

Claim 16 has been cancelled, claims 14, 15, 18, and 19, have been amended, and claims 29-31 are newly submitted. Claims 1-15 and 17-31 are pending, claims 1-13 and 23-28 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim in paper #9. Claims 14, 15, 17-22, and 29-31 are under current examination.

This application contains claims (1-13, 23-28) drawn to an invention nonelected without traverse in Paper No. 8. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in paper #11 would be addressed to the extent that they apply to current rejection.

Claim Objections

Claim 21 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 21 depends from claims 19 and 20, which are now limited to a hybrid cell comprises at least one cell

selected from the group consisting of a macrophage, a dendritic cell and an antigen presenting cell that lacks an accessory factor required to generate a positive immune response, which is the same in scope of claim 21. Accordingly, claim 21 fails to further limit the subject matter of a previous claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14, 17, 18 stand rejected and claims 29 and 30 are newly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The amended claims are now limited to purifying the resultant hybrid by cell sorting comprising bringing at least two different cells into contact under conditions that promote cell fusion and then purifying the resultant hybrid by cell sorting without antibiotic or metabolic selection. Given the broadest reasonable interpretation, the claims embrace a method of sorting for hybrid cells without fluorescent dye staining. However, the specification fails to teach the means and criteria for sorting hybrid cells without dye stain. The only means disclosed in the specification is first labeling the fusion partners with a fluorescent or cyanine dye, and then sorting for double stained cells. Accordingly, the specification fails to provide an enabling disclosure to support the

full scope of the claims. One of skilled in the art could not practice the invention commensurate with the scope of the claims without undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The amendment to claims necessitated modification of previous rejections that appear below.

Claims 14, 15, 17-19, and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Gong et al* (Nature 1997;3:558-561, IDS), and *Koolwijk et al* (Hybridoma 1988;7:217-225), as evidenced by *Abbas et al* (Cell Mol Immunol 1999).

Gong et al teach the fusion between cultivated resting dendritic cells and MC38/MUC1 tumor cells, they bring the two different types of cells into contact and fusing with PEG. Because the resting dendritic cells are lacking or absent of accessory factor B7 expression, they meet claim limitation (see fig. 8-4, *Abbas et al*). For the hybrid cell selection, *Gong et al* use HAT plating, which considered as a metabolic selection, and cell surface marker identification, which involves phenotype fluorescent cell sorting (fig. 1a). *Gong et al* use metabolic selection combined with cell sorting.

Koolwijk et al teach a method of preparing and purifying a hybrid cell, comprising contacting a first cell with a green fluorescent, contacting a second cell with a red fluorescent, bringing the two different cells into contact and fusing the cells with polyethylene glycol 4000. The double fluorescent stained hybrid cells were then sorted by FACS (e.g. abstract). The process taught by *Koolwijk et al* does not involve antibiotic or metabolic selection. *Koolwijk et al* go on to teach, "THE MAJOR ADVANTAGE OF THIS METHOD OF HYBRID HYBRIDOMA ISOLATION OVER THE METHOD USING MUTANT PHENOTYPES AND A BIOCHEMICAL SELECTION AFTER FUSION IS THE FAST ISOLATION PROCEDURE. NO TIME-CONSUMING ISOLATION OF THE MUTANT PHENOTYPES BEFORE FUSION IS NEEDED. AFTER FUSION, THE BIOCHEMICAL SELECTION PROCEDURE IS NOT NECESSARY" (see Introduction and Discussion). Although the two different cells used are different hybridoma cells, hybridoma cells are the fusion product of tumor cells and B-lymphocytes, which is a type of antigen

Art Unit: 1632

presenting cells. However, the fusion partner of the hybrids taught by *Koolwijk et al* does not comprise an individual antigen-presenting cell without fused with a tumor cell.

Evidently, selecting and purifying hybrid cells using different color of dyes by cell sorting is well known in the art as taught by *Koolwijk et al*, fusing tumor cells and dendritic cells to make a hybrid cell for anti-tumor effect is also well-known in the art as taught by *Gong et al*. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the methods taught by *Koolwijk et al*, in the process for selection and purification of dendritic-tumor cell hybrids with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to employ or modify the method because it requires fewer steps for the hybrid cell selection. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

In paper #11, applicants argue that *Gong et al* teaches away from the present invention because *Gong et al* utilized classical selection methods to identify fused cells. The argument is fully considered but it is not persuasive because the reference of *Gong et al* is applied to show that the skilled artisan knows making a hybrid cell between dendritic and tumor cells, not for the cell selection or purification process; whereas the selection process is taught by *Koolwijk et al*. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge

Art Unit: 1632

generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 14, 15, 17-22, and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Koolwijk et al* (Hybridoma 1988;7:217-225) and *Gong et al* (Nature 1997;3:558-561, IDS) as applied to claims 14, 15, 17-19, 29-31 above, further in view of *Horen et al* (US 4,859,584, IDS) and *Deka et al* (US 6,197,593).

Koolwijk et al and *Gong et al* teach selecting and purifying the DC-tumor hybrid cells by labeling fusion partner cells with different fluorescent dyes and sorting the double-fluorescent cells after fusion of two cells as discussed above. The combined teaching of *Koolwijk et al* and *Gong et al* do not teach using cyanine dyes in the FACS.

Horen et al teach the type of long chain cyanine dyes that are less toxic to cells, stable in viable cells, and staining the cell membrane of variety of cells, thus more suitable for *in vitro* and particularly *in vivo* use (columns 1 & 2). *Deka et al* teach that cyanine dyes (SYTO and TOTO serials) could be used for distinguishing between different cell populations (abstract and figures).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Koolwijk et al* and *Gong et al*, by simply substituting the red and green fluorescents with cyanine dyes for cell staining as taught by *Horen et al* and *Deka et al* with a reasonable expectation of success. The

ordinary skilled artisan would have been motivated to modify the method because the advantage of cyanine dyes taught by *Horen et al.* Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

In response to applicant's argument that the invention is not obvious over the combined teachings cited above because there is no suggestion to combine the references, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
December 18, 2002


DEBORAH J. REYNOLDS
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600